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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/825,186 | 04/16/2004 | John Zeng Hui Zhang | 57953/1221 (ZHA01-01) | 8260 |

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| EXAMINER | |
|---|---|
| SKOWRONEK, KARLHEINZ R | |
| ART UNIT | PAPER NUMBER |
| 1631 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/825,186 | ZHANG ET AL. | |
| | Examiner | Art Unit | |
| | KARLHEINZ R. SKOWRONEK | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4,7-16,20-27 and 30-44* is/are pending in the application.

4a) Of the above claim(s) *39-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-16,20-27 and 30-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Status*

Claims 1-4, 7-16, 20-27, and 30-44 are pending.

Claims 5-6, 17-19, and 28-29 are cancelled.

Claims 39-44 are withdrawn as being directed to a non-elected invention.

Claims 1-4, 7-16, 20-27, and 30-38 have been examined.

### *Claim Rejections - 35 USC § 112*

### *Response to Arguments*

Applicants' arguments, see Remarks p. 14, filed 14 May 2008, with respect to the rejection of claims 1, 16, and 27 under 35 USC 112, second paragraph have been fully considered. The rejection of claims 1, 16, and 27 has been withdrawn in view of the amendments to the claims.

Applicants' arguments, see Remarks p. 14, filed 14 May 2008, with respect to the rejection of claim 7 under 35 USC 112, second paragraph have been fully considered. The rejection of claim has been withdrawn in view of the amendments to the claim.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 16 and 20-26 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to a computer readable medium having instructions stored thereon. Interpreted broadly,

reasonably, the claims may have an embodiment in which the instructions are directed to non-functional descriptive material. In an alternative interpretation, the claims may have an embodiment in which the claims are directed to functional descriptive material Thus, the instructions as claimed encompass both functional as well as non-functional descriptive material. Non-functional descriptive material stored on a tangible computer readable medium is not eligible for patent protection because the non-functional descriptive material itself does not impart functionality and thereby become functionally interrelated to the computer , the claim is rejected under 35 USC 101. As currently recited, the claimed instructions are not required to be in a computer executable form. The lack of a computer executable form results in instructions that do not impart functionality and are not functiionaly interrelated to the computer. If the claim were amended to recite “computer-executable instructions”, the rejection may be overcome.

***Response to Arguments***

Applicant's arguments filed 14 April 2008 have been fully considered but they are not persuasive. Applicant argues the claims are statutory even if some of the instructions are directed non functional material. The argument is not persuasive. Under a broad but reasonable interpretation of the claims, the claims represent embodiments in which all of the instructions are directed non-functional material, embodiments in which all of the instructions are directed to functional descriptive material and embodiments in which some of the instructions are directed to functional descriptive material and some of the instructions are directed to non-functional descriptive material. Because the claims can be interpreted to be directed to an embodiment in which all the

instructions are non-functional descriptive material, the claim is rejected under 35 USC 101 as non-statutory. As currently recited, the claimed instructions are not required to be in a computer executable form. The lack of a computer executable form results in instructions that do not impart functionality and are not functiionaly interrelated to the computer. If the claim were amended to recite "computer-executable instructions", the rejection may be overcome. The rejection is maintained.

***Claim Rejections - 35 USC § 112***

## First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

WRITTEN DESCRIPTION

Claims 1-4, 7-16, 20-27, and 30-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a LACK OF WRITTEN DESCRIPTION rejection.

Claims 1-4, 7-16, 20-27, and 30-38 recite conjugated caps, which are not described by the specification such that one skilled in the art would be apprised of the structure intended. [0038] discloses that each pair of caps has a first cap member and a second cap member while [0040] discloses that caps are atoms or radicals that bond with a

severed portion of a molecule. Neither [0038] nor [0040] discloses what the relationship of two radicals or atoms (that bond to a severed portion) are to each other such that the two caps are considered to be “conjugated.” The specification does not define the terms "conjugated" and “conjugate”. Confusingly, the terms are used inconsistently throughout the specification. [0041] discloses that a first cap may be $NH^+_3$ and that “other caps” may be $R_NC_\alpha H_2$. [0041] does not disclose or exemplify what the conjugate (second cap member) which corresponds to a first cap member of $NH^+_3$ actually IS. Neither the figures nor the examples show, exemplify or otherwise describe what is intended by a “conjugated cap” such that one skilled in the art would know what relationship caps must have to each other to be considered conjugated. Conjugated caps could be a distinct molecular species, which is implied at [0044], lines 12-13. Alternatively, conjugated caps could refer to caps that have been conjugated to fragments as implicitly indicated in [0039]. In a third alternative, conjugated caps could refer to cap pairs in which a first cap and a second cap are conjugates of one another as suggested in [0038]. As the structure of a pair of conjugated caps is not described or exemplified anywhere such that one skilled in the art would know what structures are intended and what relationship is required for “conjugated caps”, the claims lack a full and complete written description and are rejected.

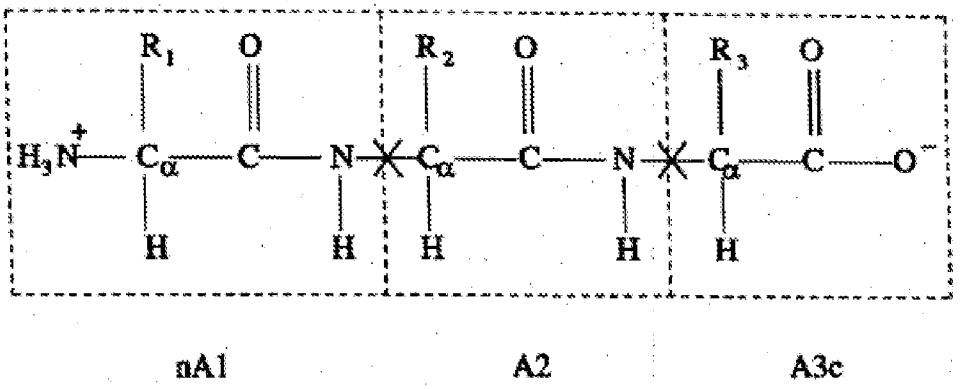
***Response to Arguments***

Applicant's arguments filed 14 April 2008 have been fully considered but they are not persuasive. Applicant argues that from the guidance provided at [0040-0042] one

skilled in the art would know how conjugate caps are determined and the relation between the conjugate cap and the severed molecule. The argument is not persuasive.

Applicant attempts to explain in view of figure 1, that the first cap on the $A_2$ fragment, $C^1_{ap}$, should represent everything to the right side of the first decomposition point. Referring to figure 1, reproduced below, applicant indicates that the first decomposition point occurs between nA1 and A2, thus everything to the right side of the decomposition point is $C_\alpha H(R_2)CC\ NHC_\alpha H(R_3)COO^-$.

Figure 1




However, applicants' argument is in contrast with what the specification actually teaches at [0038]. Specifically, the specification teaches that in Fig. 1, cap $c^1_{ap}$ is used to terminate the right end of molecule fragment nA1 at the first decomposition point, while its conjugate cap $c^{1*}_{ap}$, is employed to terminate the left end of molecule fragment A2; similarly, cap $c^2_{ap}$, is employed to terminate the right end of molecule fragment A2 at the second decomposition point, while its conjugate cap $c^{2*}$, is used to terminate the left end of molecule fragment A3c. The specification continues in [0039] to show in Fig. 1, the left-hand molecule portion contains molecule fragment nA1 and cap member $c^1_{ap}$;

the middle molecule portion contains molecule fragment A2 and cap members $c^{1*}_{ap}$ and $c^{2}_{ap}$; and the right-hand molecule portion contains molecule fragment $A_3c$ and cap member $c^{2*}_{ap}$. While [0040] does indicate referring to figure 1 that the cap $c^{1}_{ap}$ should closely represent the electronic effect of everything to the right side of the first decomposition point. The specification does not describe how this is accomplished, but does indicate at [0041] that $c^{i}_{ap}$ could be $R_{i+1}CH_2$. However, inconsistent with the example from [0041] in which $c^{1*}_{ap}$ represents the electronic effect of $nA_1$ ($NH_3R_1C\alpha HCONH$), [0042] indicates that $c^{1*}_{ap}$ is $NH_2$. In paragraph [0042], the specification shows that after a molecule has been decomposed and capped with conjugated caps to create a plurality of molecular portions, the molecular portions may be used to measure intermolecular interaction energy. Thus from the specification it appears that each molecular portion may contain up to 2 caps which are conjugated to the molecule fragment, such that for any molecule fragment $A_i$, the molecular portion used in the intermolecular interaction energy calculation is composed of cap $c^{i-1*}_{ap}$, $A_i$, and $c^{i}_{ap}$. At [0064], consistent with [0042] and inconsistent with [0041], $c^{1*}_{ap}$ is defined to be $NH_2$; $C^{1-i*}_{ap}$ is defined to be $NH_2$; $A_i$ is defined to be $R_iC_aHCOHN$; and $c^{i}_{ap}$ is defined to be $R_{i+1}C_aH_2$.

In the addendum, the applicants provide a clarification of the molecular fragmentation with conjugate caps approach in which a molecule p is decomposed into fragments A and B. The fragments are then conjugated, coupled or fused with another molecular entity c or c* to form the molecular species A-c and B-c*. A third species is formed from the coupling of molecular entities c and c* to form c-c*. The addendum

defines conjugate caps to be the pair of caps that cap (c and c*) the fragments formed as a result of cutting the molecule P and that are coupled or fused.

Comparison of the addendum to the specification reveals significant similarities and differences. First, the description of the c and c* are consistent with the example of a first cap $c^{1}_{ap}$ and a second cap $c^{1*}_{ap}$. Second, the coupling of the cap pairs c and c* to form c-c* is distinct from the molecular species formed in [0064]. Third, the addendum is consistent with the example in [0040] insofar that c appears to represent the electronic environment to the right of the decomposition point and is coupled to the fragment to the left of the decomposition point whereas c* appears to represent the electronic environment to the left of the decomposition point and is coupled to the fragment to the right of the decomposition point. Fourth, the addendum provides a definition of conjugate caps, the specification does not provide a definition for conjugate caps rather it uses the term inconsistently to refer different molecular species. Fifth, it is clear from the figure provided in the addendum that if the a molecular interaction energy were calculated for the molecular portion A-c and c-c* as directed in the specification to subtract the interaction of coupled caps from the molecular portion would result in an energy representing the molecular fragment to the left of the $C_{\alpha}$ of fragment A. However as calculated at [0064], the result of the molecular interaction calculation would result in an interaction energy representative of the $C_{\alpha}$ and the R group. Sixth, the addendum defines c and c* as small molecular entities. The specification shows that a cap should preserve the property of the bond being severed and mimic as much as possible the effect of the severed molecular part removed from the remaining severed molecular part

[0040]. From the limited guidance provided in the specification, conjugate cap pairs appear to have a molecule composition comprising more than small molecular entity. Conjugate caps are not explicitly defined in the disclosure. The specification does not define the terms "conjugated" and “conjugate”. Confusingly, the terms are used inconsistently throughout the specification. Therefore based on the teaching in the specification, caps and conjugate caps are distinct entities. In the claims it is currently recited any pair of caps may be used to produce the molecular portions, where a molecular portion comprises a fragment of the first molecule and at least a cap. The specification does not provide written support that any cap can be attached to any severed molecule. Rather a cap preserves the bond property and mimics the effect of the severed part [0040]. Applicant’s argument similarly reflect the relation of the cap pair to the molecule being severed, in that any cap may be chosen provided that reasonably mimics the molecular fragment that it is substituted for (remarks, p. 12, paragraph 2).

[0041] does not further clarify the relation between caps and conjugated caps. In the example put forth in [0041] indicates the first molecular cap as $NH_3^+$. Other caps are indicated as $R_{i+1}C_\alpha H_2$ and $NH_2$ which are also not caps as defined by applicant. In [0042], the cap terminology is replaced with “conjugate caps”. The remainder of [0042] is directed to calculating interaction energies of molecular portions.

Paragraphs [0040-0042] do not describe the relation between caps and conjugated caps such that one skilled in the art would know what structures are intended and what relationship is required for “conjugated caps”.

NEW MATTER

Claims 1-4, 7-16, 20-27, and 30-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

Claim 1, 16, and 27 are directed to a method of calculating intermolecular interaction energy between two molecules comprising a step of coupling a pair of caps to form one or more conjugated caps. The disclosure as originally filed does not provide written support for the limitation of coupling each pair of caps to form conjugated caps. The specification discloses, at [0064], the formation of an artificial molecular species by coupling conjugate caps. Line 14-15 of [0064] recites that "the conjugate caps can be coupled to form artificial species whose interaction with the external molecule will be calculated to cancel out the artificial interaction with the molecular caps". The molecular species described at [0064] is distinct from a conjugated cap because the artificial species is formed from the coupling of conjugate caps. As currently claimed, cap pairs are coupled to form conjugated caps. The specification, by way of an example at lines 20-23 of [0064], shows that cap pairs $C^{i-1*}_{ap}$ and $C^{i}_{ap}$ used to bound the left and right sides of the fragment $A_i$ and that the caps $C^{i*}_{ap}$ $C^{i}_{ap}$ are coupled to form a molecular species. However, [0064] is completely silent regarding cap $C^{i*}_{ap}$. Paragraph [0064] does not describe the coupling of caps to form conjugated caps. The inconsistent use of

terms to refer to the various molecular species further confuses the distinction between "conjugate caps", "conjugated caps", and "caps".

### *Response to Arguments*

Applicant's arguments filed 14 April 2008 have been fully considered but they are not persuasive. Applicant argues that conjugate caps can be coupled. The argument is persuasive. [0064] shows the conjugate caps can then be coupled to form artificial molecular species whose interaction with the external molecule will be calculated to cancel out the artificial molecular interaction with individual conjugate caps. Paragraph [0064] is completely silent with respect to the formation of conjugated caps from cap pairs. Therefore, the coupling of caps to generate a conjugated cap is new matter.

### *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571) 272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

25 July 2008

/K. R. S./
Examiner, Art Unit 1631
/John S. Brusca/
Primary Examiner, Art Unit 1631